

CLAIMS

1. A substantially pure *Yatapoxvirus* immunomodulatory polypeptide.

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2. The polypeptide of claim 1, wherein said polypeptide is derived from yaba monkey tumor virus.

3. The polypeptide of claim 1, wherein said polypeptide is derived from

10 tanapox virus.

4. The polypeptide of claim 1, wherein said polypeptide comprises an amino acid sequence that encodes an identifiable signal sequence.

5. The polypeptide of claim 1, wherein said polypeptide is selected from the group consisting of a chemokine binding polypeptide, a cytokine binding polypeptide, an immunomodulator, and an anti-inflammatory polypeptide.

6. The polypeptide of claim 5, wherein said chemokine is selected from the group consisting of human interferon- γ , human interleukin-2, and human interleukin-5.

7. The polypeptide of claim 1, wherein said polypeptide is glycosylated.

8. The polypeptide of claim 1, wherein said polypeptide has anti-cytokine activity.

9. The polypeptide of claim 1, wherein said polypeptide comprises an amino acid sequence that is substantially identical to the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.

10. The polypeptide of claim 9, wherein said polypeptide comprises the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.

11. A substantially pure *Yatapoxvirus* nucleic acid molecule, wherein said nucleic acid molecule encodes a *Yatapoxvirus* immunomodulatory polypeptide.

12. The nucleic acid molecule of claim 11, wherein said nucleic acid molecule is selected from the group consisting of genomic DNA, cDNA, and mRNA.

13. The nucleic acid molecule of claim 11, wherein said nucleic acid molecule comprises a nucleotide sequence that encodes a polypeptide with an identifiable signal sequence.

14. The nucleic acid molecule of claim 11, wherein said nucleic acid molecule encodes a yaba monkey tumor virus polypeptide.

15. The nucleic acid molecule of claim 11, wherein said nucleic acid molecule encodes a tanapox virus polypeptide.

16. The nucleic acid molecule of claim 11, wherein said nucleic acid molecule encodes a polypeptide comprising an amino sequence that is substantially identical to the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.

17. The nucleic acid molecule of claim 16, wherein said nucleic acid molecule encodes a polypeptide comprising the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.

18. The nucleic acid molecule of claim 11, wherein said nucleic acid molecule comprises a nucleotide sequence that is substantially identical to the nucleotide sequence of SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 7.

19. A nucleic acid molecule having at least 50% nucleic acid sequence identity to a sequence encoding a *Yatapoxvirus* immunomodulatory polypeptide or a fragment thereof, wherein said fragment comprises at least six amino acids and said nucleic acid molecule hybridizes under high stringency conditions to at least a portion of a *Yatapoxvirus* nucleic acid molecule.

20. The nucleic acid molecule of claim 19, wherein said nucleic acid molecule has 100% complementarity to a nucleic acid molecule encoding a *Yatapoxvirus* immunomodulatory polypeptide or a fragment thereof comprising at least six amino acids, and said nucleic acid molecule hybridizes under high stringency conditions to at least a portion of a *Yatapoxvirus* nucleic acid molecule.

21. A nucleic acid molecule, wherein said nucleic acid molecule comprises a sequence that is antisense to the coding strand of a *Yatapoxvirus* nucleic acid molecule or a fragment thereof.

22. A vector comprising the nucleic acid molecule of claim 11.

23. The vector of claim 22, wherein said vector is a gene therapy vector.

24. A cell comprising the vector of claim 22.

25. The vector of claim 22, wherein said nucleic acid molecule is operably linked to regulatory sequences for expression of a *Yatapoxvirus* polypeptide and wherein said regulatory sequences comprise a promoter.

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26. The cell of claim 24, wherein said cell is selected from the group consisting of a human cell, a primate cell, and a rodent cell.

10 27. A non-human transgenic animal comprising the nucleic acid molecule of claim 11.

28. A cell from the non-human transgenic animal of claim 27.

15 29. A non-human transgenic animal having a knockout mutation in one or both alleles encoding a polypeptide substantially identical to a *Yatapoxvirus* polypeptide.

30. An antibody that specifically binds to a *Yatapoxvirus* polypeptide.

20 31. The antibody of claim 30, wherein said polypeptide comprises an amino acid sequence that is substantially identical to the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6.

25 32. A probe for analyzing a *Yatapoxvirus* gene or a *Yatapoxvirus* gene homolog or fragment thereof, said probe having at least 50% nucleotide sequence identity to a sequence encoding a *Yatapoxvirus* polypeptide or fragment thereof, wherein said fragment comprises at least six amino acids, and said probe hybridizes under high stringency conditions to at least a portion of a *Yatapoxvirus* nucleic acid molecule.

33. The probe of claim 32, wherein said probe has 100% complementarity to a nucleic acid molecule encoding a *Yatapoxvirus* polypeptide or fragment thereof, wherein said fragment comprises at least six amino acids, and said probe hybridizes under high stringency conditions to at least a portion of a *Yatapoxvirus* nucleic acid molecule.

34. A method of detecting a *Yatapoxvirus* polypeptide in a sample, said method comprising contacting said sample with the antibody of claim 30, and assaying for the binding of said antibody to said polypeptide.

35. A method of detecting a *Yatapoxvirus* gene or a *Yatapoxvirus* gene homolog or fragment thereof in a cell, said method comprising contacting the nucleic acid molecule of claim 11 or a fragment thereof, wherein said fragment is greater than about 18 nucleotides in length, with a preparation of genomic DNA from said cell, under hybridization conditions providing detection of DNA sequences having about 50% or greater nucleotide sequence identity to SEQ ID NO: 3, SEQ ID NO: 5, or SEQ ID NO: 7.

36. A method of identifying an immunomodulatory *Yatapoxvirus* gene or a *Yatapoxvirus* immunomodulatory gene homolog or fragment thereof comprising:

- (a) providing a mammalian cell sample;
- (b) introducing into said cell sample a candidate gene;
- (c) expressing said candidate gene; and
- (d) determining whether said candidate gene elicits an alteration in the level of immune function in said cell sample, wherein an alteration in the level of immune function identifies said immunomodulatory *Yatapoxvirus* gene or said *Yatapoxvirus* immunomodulatory gene homolog, or fragment thereof.

37. A method for identifying a test compound that modulates the expression or activity of a *Yatapoxvirus* polypeptide, said method comprising contacting said *Yatapoxvirus* polypeptide with said test compound, and determining the effect of said test compound on said *Yatapoxvirus* polypeptide expression or activity.

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38. A method of targeting proteins for secretion from a cell, comprising attaching an identifiable signal sequence selected from a *Yatapoxvirus* polypeptide to a protein of interest, wherein said protein of interest is secreted from said cell.

10 39. A method of immunomodulation in a mammal, said method comprising: administering to said mammal a therapeutically effective amount of a *Yatapoxvirus* polypeptide or fragment thereof, wherein said polypeptide has an immunomodulatory effect in said mammal.

15 40. A method of immunomodulation in a mammal, said method comprising: administering to said mammal a therapeutically effective amount of a compound that modulates the activity of a *Yatapoxvirus* polypeptide, wherein said compound has an immunomodulatory effect in said mammal.

20 41. A method of treating a mammal having an immunomodulatory disorder, said method comprising: administering to said mammal a therapeutically effective amount of a compound that modulates the activity of a *Yatapoxvirus* polypeptide, wherein said compound has an immunomodulatory effect in said mammal.

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42. A pharmaceutical composition comprising at least one dose of a therapeutically effective amount of a *Yatapoxvirus* polypeptide or fragment thereof, in a pharmaceutically acceptable carrier, said composition being formulated for the treatment of an immunomodulatory disorder.

43. The method of claims 37 to 42, wherein the *Yatapoxvirus* polypeptide comprises an amino acid sequence substantially identical to the amino acid sequence of SEQ ID NO: 1, SEQ ID NO: 2, SEQ ID NO: 4, or SEQ ID NO: 6, and
5 fragments and analogs thereof.

44. The method of claim 39 or 40, wherein said immunomodulation is selected from the group consisting of immunosuppression, immunostimulation, cell proliferation, apoptosis, decreasing T cell stimulation, and decreasing
10 inflammation in a mammal.

45. The method of claims 39 to 41, wherein said mammal is a human.

46. The method of claims 39 to 41, wherein said mammal has a condition
15 selected from the group consisting of acute inflammation, rheumatoid arthritis, transplant rejection, asthma, inflammatory bowel disease, uveitis, restenosis, multiple sclerosis, psoriasis, wound healing, lupus erythematosus, allergic rhinitis, atopic dermatitis, food allergies, type 1 insulin-dependent diabetes mellitus, deramatitis, meningitis, thrombotic thrombocytopenic purpura, Sjogren's
20 syndrome, encephalitis, leukocyte adhesion deficiency, rheumatic fever, Reiter's syndrome, psoriatic arthritic, progressive systemic sclerosis, primary biliary cirrhosis, pemphigus, pemphigoid, necrotizing vasculitis, mayasthenia gravis, lupus erythmatosus, polymyositis, sarcoidosis, granulomatorsis, vasculitis, pernicious anemia, CNS inflammatory disorder, antigen-antibody complex
25 mediated diseases, autoimmune hemolytic anemia, Hashimoto's thyroiditis, Graves disease, habitual spontaneous abortions, Reynard's syndrome, glomerulonephritis, dermatomyositis, chronic active hepatitis, celiac disease, autoimmune complications of AIDS, atrophic gastritis, ankylosing spondylitis, Addison's disease, psoriasis, penphigus vularis, Behcet's syndrome, acute

respiratory distress syndrome (ARDS), ischemic heart disease, atherosclerosis, post-dialysis syndrome, leukemia, acquired immune deficiency syndrome septic shock and other type of acute inflammation, and lipid histiocytosis.

47. A kit for the analysis of a *Yatapoxvirus* nucleic acid molecule, said kit comprising a nucleic acid molecule probe for analyzing a *Yatapoxvirus* nucleic acid molecule present in a test subject.

48. A kit for the analysis of a *Yatapoxvirus* polypeptide, said kit comprising an antibody for analyzing a *Yatapoxvirus* polypeptide present in a test subject.

49. A method for identifying a test compound that modulates the expression or activity of a polypeptide comprising an amino acid sequence that is substantially identical to the amino acid sequence of SEQ ID NO: 8, said method comprising contacting said polypeptide with said test compound, and determining the effect of said test compound on said polypeptide expression or activity.

50. A method of targeting proteins for secretion from a cell, comprising attaching an identifiable signal sequence selected from a polypeptide comprising an amino acid sequence that is substantially identical to the amino acid sequence of SEQ ID NO: 8 to a protein of interest, wherein said protein of interest is secreted from said cell.

51. A method of immunomodulation in a mammal, said method comprising: administering to said mammal a therapeutically effective amount of a polypeptide comprising an amino acid sequence that is substantially identical to the amino acid sequence of SEQ ID NO: 8, or fragment thereof, wherein said polypeptide has an immunomodulatory effect in said mammal.

52. A method of immunomodulation in a mammal, said method comprising:
administering to said mammal a therapeutically effective amount of a compound
that modulates the activity of a polypeptide comprising an amino acid sequence
that is substantially identical to the amino acid sequence of SEQ ID NO: 8,
5 wherein said compound has an immunomodulatory effect in said mammal.

53. A method of treating a mammal having an immunomodulatory disorder,
said method comprising:
administering to said mammal a therapeutically effective amount of a compound
10 that modulates the activity of a polypeptide comprising an amino acid sequence
that is substantially identical to the amino acid sequence of SEQ ID NO: 8,
wherein said compound has an immunomodulatory effect in said mammal.

54. A pharmaceutical composition comprising at least one dose of a
15 therapeutically effective amount of a polypeptide comprising an amino acid
sequence that is substantially identical to the amino acid sequence of SEQ ID NO:
8, or fragment thereof, in a pharmaceutically acceptable carrier, said composition
being formulated for the treatment of an immunomodulatory disorder.

20 55. The method of claims 49 to 54, wherein the polypeptide has an amino acid
sequence of SEQ ID NO: 8.

56. The method of claim 51 or 52, wherein said immunomodulation is selected
from the group consisting of immunosuppression, immunostimulation, cell
25 proliferation, apoptosis, decreasing T cell stimulation, and decreasing
inflammation in a mammal.

57. The method of claims 51 to 53, wherein said mammal is a human.

58. The method of claim 51 to 53, wherein said mammal has a condition selected from the group consisting of acute inflammation, rheumatoid arthritis, transplant rejection, asthma, inflammatory bowel disease, uveitis, restenosis, multiple sclerosis, psoriasis, wound healing, lupus erythematosus, allergic rhinitis, atopic dermatitis, food allergies, type 1 insulin-dependent diabetes mellitus, deramatitis, meningitis, thrombotic thrombocytopenic purpura, Sjogren's syndrome, encephalitis, leukocyte adhesion deficiency, rheumatic fever, Reiter's syndrome, psoriatic arthritic, progressive systemic sclerosis, primary biliary cirrhosis, pemphigus, pemphigoid, necrotizing vasculitis, mayasthenia gravis, lupus erythmatusus, polymyositis, sarcoidosis, granulomatorsis, vasculitis, pernicious anemia, CNS inflammatory disorder, antigen-antibody complex mediated diseases, autoimmune hemolytic anemia, Hashimoto's thyroiditis, Graves disease, habitual spontaneous abortions, Reynard's syndrome, glomerulonephritis, dermatomyositis, chronic active hepatitis, celiac disease, autoimmune complications of AIDS, atrophic gastritis, ankylosing spondylitis, Addison's disease, psoriasis, penphigus vularis, Behcet's syndrome, acute respiratory distress syndrome (ARDS), ischemic heart disease, atherosclerosis, post-dialysis syndrome, leukemia, acquired immune deficiency syndrome septic shock and other type of acute inflammation, and lipid histiocytosis.